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(FILE 'USPAT' ENTERED AT 14:57:25 ON 11 SEP 1998)

L1	1 S 5447851/PN
L2	1 S 5731168/PN
L3	101 S FC(5A) (FUSION OR CHIMER?)
L4	66 S L3(P) (IG?)
L5	1 S 5395760/PN
L6	0 S L5 AND (DIMER? OR MULTIMER?)
L7	1 S L5 AND FUSION?
L8	31925 S DIMER? OR MULTIMER? OR HETEROMULTIM? OR HOMOMULTIM?
L9	1392 S L8(6A) (PROTEIN? OR POLYPEPTID? OR RECEPTOR?)
L10	2024 S L8/AB OR L8/CLMS
L11	82 S L10(6A) (PROTEIN? OR POLYPEPTID? OR RECEPTOR?)
L12	81 S L11 NOT L4

5,116,964 -16
+3
5,428,130 1-2
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5,914,47

Late

US PAT NO: 5,605,690 [IMAGE AVAILABLE] L4: 48 of 66
DATE ISSUED: Feb. 25, 1997
TITLE: Methods of lowering active TNF-.alpha. levels in mammals
using tumor necrosis factor receptor
INVENTOR: Cindy A. Jacobs, Seattle, WA
Craig A. Smith, Seattle, WA
ASSIGNEE: Immunex Corporation, Seattle, WA (U.S. corp.)
APPL-NO: 08/385,229
DATE FILED: Feb. 8, 1995
REL-US-DATA: Continuation of Ser. No. 946,236, Sep. 15, 1992,
abandoned, which is a continuation-in-part of Ser. No.
523,635, May 10, 1990, Pat. No. 5,395,760, which is a
continuation-in-part of Ser. No. 421,417, Oct. 13, 1989,
abandoned, which is a continuation-in-part of Ser. No.
405,370, Sep. 11, 1989, abandoned, which is a
continuation-in-part of Ser. No. 403,241, Sep. 5, 1989,
abandoned. *no basis for dimer!*
INT-CL: [6] A61K 39/395; A61K 38/00; C12P 21/04; C07K 14/715
US-CL-ISSUED: 424/134.1; 435/69.7; 514/12, 825; 530/350, 387.3, 866, 868
US-CL-CURRENT: 424/134.1; 435/69.7; 514/12, 825; 530/350, 387.3, 866, 868
SEARCH-FLD: 435/69.1, 69.7, 172.3, 240.27; 424/85.1, 134.1; 530/351,
387.3, 868; 935/9, 12, 15
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ART-UNIT: 186
PRIM-EXMR: Lila Feisee
ASST-EXMR: John Lucas
LEGAL-REP: Stephen L. Malaska

ABSTRACT:

A method for treating TNF-dependent inflammatory diseases in a mammal by administering a TNF antagonist, such as soluble TNFR.

6 Claims, 7 Drawing Figures

DRAWING DESC:

DRWD(2)

FIG. 1 shows the dimeric structure of the recombinant human TNFR/**Fc fusion** protein. The primary translation product of the plasmid coding for rhu TNFR/Fc is a single molecule of soluble TNFR linked to single chain of Fc derived from human **IgG1**. Following translation, but prior to secretion, this fusion molecule dimerizes via 3 cysteine residues in the Fc region to form. . .

DETDESC:

DETD(24)

A . . . either or both of the immunoglobulin molecule heavy and light chains and having unmodified constant region domains. For example, chimeric TNFR/**IgG**.sub.1 may be produced from two chimeric genes--a TNFR/human .kappa. light chain chimera (TNFR/G.sub..kappa.) and a TNFR/human .gamma..sub.1 heavy chain chimera. . . displayed bivalently. Such polyvalent forms of TNFR may have enhanced binding affinity for TNF ligand. One specific example of a TNFR/**Fc fusion** protein is disclosed in SEQ ID NO:3 and SEQ ID NO:4. Additional details relating to the construction of such chimeric. . .